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for a long time after the cure of the gonorrhœa. It seems that this secondary infection, as like as not with sulphonamide resistant organisms, is well nigh inevitable, but it is debatable whether the condition will clear up properly without adequate local treatment. My own experience leads me to think that usually it will not do so, and in many of my own cases the initial week of chemotherapy is followed by two, three or four weeks of local treatment before the cervix and its secretion approach the normal. The subject of non-gonococcal vaginal discharges to be discussed at a future meeting of this society, has a direct bearing on the problem of non-gonococcal urethritis in men.

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NON-GONOCOCCAL URETHRITIS *

By I. N. ORPWOOD-PRICE, M.R.C.S., L.R.C.P., D.P.H.

I UNDERSTAND that there has been a high incidence of non-gonococcal urethritis in the Services, more particularly in the Royal Air Force. In order to gain some idea as to whether this increase has its counterpart in civilian life I have examined the records of two clinics—Whitechapel and University College Hospital. The figures which are for July–December, 1941 inclusive, are as follows :—

PROPORTION OF GONOCOCCAL AND NON-GONOCOCCAL URETHRITIS

	Whitechapel Clinic	University College Hospital Clinic
Non-gonococcal urethritis		
Total cases	73 (21·3%)	26 (17%)
Cases with previous history of gonorrhœa	34 (46%)	8 (30·8%)
Gonococcal urethritis	270 (78·7%)	127 (83%)

The percentage figures of these two clinics agree fairly well, in spite of the fact that the patients of each are, on the whole, drawn from different social strata. They do not show any appreciable increase in the number of cases suffering from non-gonococcal urethritis. An interesting point is that, almost half of the patients suffering from non-gonococcal urethritis will admit a previous attack of gonorrhœa. (According to Pelouze, this state of affairs obtains in U.S.A., 333 N.V.D. urethritis, of which 193 admit previous gonorrhœa.)

* An address to the Medical Society for the Study of Venereal Diseases, May 30th, 1942.

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The causes of non-gonococcal urethritis are well known but may be recapitulated.

- (1) Asparagus, strawberries, cress.
- (2) Over indulgence in drugs such as cantharides.
- (3) Foreign bodies in the urethra, *e.g.*, calculus.
- (4) Trauma due to faulty instrumentation.
- (5) Chemicals used as a prophylactic against gonorrhœa.
- (6) Various organisms such as staphylococci, diphtheroids, coliform bacillus and streptococci, which cause a urethritis *per se* or as a sequel to attack of gonorrhœa.
- (7) Intra-urethral syphilitic chancres.
- (8) Urethral strictures,
- (9) Infection of the prostate gland and seminal vesicles.
- (10) Infection of the genito-urinary tract by various organisms including the tubercle bacillus.
- (11) Excessive coitus.
- (12) Spermatorrhœa and prostatorrhœa.

I have not mentioned *Trichomonas* as a cause of non-gonococcal urethritis as I have never seen a case.

Since the majority of urethral discharges are gonococcal in origin, the diagnosis of a non-gonococcal urethritis is usually one of exclusion. On examining case records of urethral discharges, it will be seen that most cases of gonorrhœa have usually been easily separated out, but that there are a large group which require careful investigation before a diagnosis can be made.

How the laboratory can help the clinician depends primarily on the clinicians for some are satisfied with an occasional urethral film and ignore cultures and serum tests. In the front rank of these, I place serum tests and I would remind you not to forget the Wassermann reaction when investigating urethral discharges. Many an intra-urethral hard chancre has been missed because a W.R. was not performed. The interpretation of the gonococcal complement fixation test is now fairly well known. I hold that a *persistently* positive reaction definitely indicates the presence of a focus of gonococcal infection. A diagnosis of non-gonococcal urethritis, however, cannot be made on the strength of a negative reaction, but it is of real help if it is persistent and is reviewed in conjunction with the clinical picture and other pathological tests.

Next, I would never omit cultures, provided a suitable medium is available. Cultures have been, and are still, discredited in some quarters, because a suitable medium has not been used. In my laboratory, during the first year of the war, gonococcal growths became uncertain and scanty, even on subculturing pure growths. On investigation, three points emerged :—

(1) *Meat* used in the preparation of broth, had, I suspect, been frozen and unfrozen several times and in consequence, the quality of the extract varied considerably.

(2) *Peptone*, also used in the preparation of broth, became unobtainable and a new source of supply had to be found. Before the war, I had always used De Witte brand (a German preparation), which had an excellent reputation. After numerous trials, I discovered a British firm who now produce peptone which is as good, if not better. I am certain that if an inferior make of peptone is used, one cannot expect the gonococcus to grow.

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(3) *Agar*. Our supply of agar also gave out and the new supply failed to set hard enough to prevent the inoculation needle tearing the surface with the gentlest handling, even when the strength was considerably increased. Since then, I have changed to a more suitable agar.

I mention these points in case they may be of help to those who are unable to obtain satisfactory growths of gonococci. When a suitable medium is available, cultures should be made. Personally, I set no great store on cultures from the *anterior urethra*, unless the gonococcus is grown, since one can often obtain from a clear or uninfected urethra, mixed growths of staphylococci, streptococci, diphtheroid bacilli and even coliform bacilli. I now consider that most of these organisms are often just as much at home in the anterior urethra as they are on the skin. I do not believe that they affect the mucous membrane of the anterior urethra, unless it has become devitalised. At this stage, may I refer to a reasonable way of taking urethral cultures. The best procedure is to wash the glans penis with sterile water and then cleanse it and the first $\frac{1}{8}$ inch of the urethra with spirit before taking any material for inoculation. In this way, extraneous organisms are almost entirely excluded.

Vesicular cultures are an essential part of the investigation of a chronic urethral discharge. The importance of this type of culture can hardly be over-estimated and yet it is not often carried out as a routine. The term, vesicular culture, is a short way of stating that the material to be inoculated is obtained from the posterior urethra, prostate gland and seminal vesicles, by so-called prostatic massage. The technique should be carried out as follows. The glans penis should be cleansed and the whole urethra washed out thoroughly with sterile water. The contents of the seminal vesicles and prostate gland should be expressed by massage and allowed to drop on to the medium contained in a Petri dish. It is best to use plates having no water of condensation on the glass and the medium should have been in the incubator for thirty minutes prior to inoculation. The inoculum can be spread over the surface of the medium by a platinum loop or by movement of the plate. After three to five days incubation, depending on the amount of growth obtained, the culture should be examined by means of the oxidase test. Any colonies showing a positive reaction should be picked off and the smear made stained by Gram's method. These smears will reveal organisms of varying types but from about 10 per cent. of the plates examined smears will show Gram-negative diplococci, morphologically indistinguishable from gonococci. These are almost invariably mixed up with staphylococci, diphtheroid bacilli and coliform bacilli, but if the smear be carefully searched, patches or islets of these Gram-negative diplococci in pure and solid formation and surrounded by the secondary organisms, will be found. Unfortunately, I have never been able to obtain these Gram-negative diplococci in pure culture, even after 30 subcultures from one colony, although I have grown subcultures, roughly 80 per cent. pure on many occasions. The explanation is that the original inoculum is, of necessity, a "wet" one, and this results in contamination by the other organisms that almost invariably accompany a chronic gonococcal infection. If one accepts these morphologically typical gonococci as

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gonococci, even in the absence of cultural proof, they help to explain many of the persistently positive gonococcal C.F.T.'s in patients who may show no clinical signs or symptoms. I believe that patients of this type from whom these organisms are obtained are often gonococcus carriers and constitute a potential menace to the community, because as in the case of a meningococcal or typhoid carrier, one has no means of ascertaining if and when the organisms will become pathological.

One gonococcus negative vesicular culture however, does not exclude the possibility of gonococci lurking in these areas. The best plan is to take three consecutive cultures and do the Gc.C.F.T. at monthly intervals whilst the patient is living a normal life and having no treatment. If all these are negative, one can be reasonably sure that no gonococci exist in these areas.

Finally one comes to smears, one of the most easy specimens to obtain and often one of the most carelessly made. All smears taken to establish the presence of any organism in its relation to a urethral discharge should be taken with the same care as a culture. I do not say that if a man has all the signs and symptoms of an acute gonococcal urethritis one need be so meticulous about the preparation of a smear, but if a non-gonococcal urethritis is suspected and information is required about the organisms present, care should be taken that in transit from the urethra to the slide, the material is not mixed with organisms from elsewhere. For example, the organisms seen in some smears made from discharges, may or may not have little or no connection with the cause of the urethritis unless the gonococcus is identified. In the same way, if one is interested in the organisms present in a prostatic infection, the whole of the urethra should be washed out with sterile water before the bead is taken. These things seem obvious but often they are ignored.

Smears also yield information by reason of their cellular content. For instance, in urethral smears taken from a patient suffering with acute urethritis, there is a type of clean cut pus cell, which means either gonorrhœa or the result of an immediate urethral reaction against a strong chemical. Usually organisms are scanty and in the case of gonorrhœa, the gonococcus is found only after a prolonged search. If such chemical treatment is persisted in, epithelial cells appear but unless the mucous membrane is roughly handled it is unusual to see many epithelial cells. Again, on the second or third day of a gonococcal infection smears reveal strands of mucus mixed with pus cells, an appearance rarely seen in non-gonococcal urethritis.

Prostatic beads are very useful as a guide to infection. Apart from finding gonococci which is quite frequent enough to warrant their use, I think that the average number of leucocytes per field seen in an evenly spread smear usually indicates the type of infection. Non-gonococcal infections evoke less reaction than gonococcal infections. Thus now, I always record the average number of leucocytes per field in units of 5, and on finding 15 or more per field, I suspect the presence of gonococci.

Once the clinician has diagnosed non-gonococcal urethritis I do not think that the laboratory is of much help. My experience of mixed vaccines of the various organisms found has not been conspicuous by successful results.

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May I say that until one has well and truly excluded the possibility of gonorrhœa, it is impossible to arrive at the diagnosis of non-gonococcal urethritis. Thus I have endeavoured to put before you what I consider to be the best laboratory methods to establish the cause of an urethral discharge.

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DISCUSSION

Dr. J. A. BURGESS said that it would assist their appreciation of these cases if there was a more definite classification. Cases of primary non-gonococcal urethritis without previous gonococcal infection could be divided into two main groups, namely, irritative and infective. The irritant group could be subdivided into sub-groups where the urethritis was due to chemical, mechanical, urinary, or sexual origin. In the infective group, there would be the various causative organisms, *e.g.*, cocci, bacilli, protozoa, metazoa or filtrable viruses.

The following interesting case belonged to the mechanical sub-group of Irritative Primary Non-gonococcal Urethritis. A man, aged 24, with an acute purulent non-gonococcal urethritis, had five or six firm palpable swellings, which he took to be infected Littre's glands. A further examination showed that the swellings were movable; on doing meatotomy 6 urethral calculi were recovered.

Major MARSHALL concurred that the incubation period was always longer than in gonorrhœa. He had examined the wives and consorts of men suffering from non-gonococcal urethritis without finding much evidence of infection comparable to that found in the male partners.

He referred to men returning after a long period overseas who were infected with gonorrhœa by their wives. In some cases it seemed certain that the man himself had infected his wife in the first instance but had become tolerant to that particular gonococcus. After a long rest, however, either the man or the gonococcus had altered, and reinfection occurred.

Dr. B. B. SHARP said that he had collected impressions on this subject over a period of 20 years. The first was that it seemed to be more prevalent in the spring or early summer. He did not know whether this was due to climate or to different seasonal activities. He also thought that quite a large proportion of these cases had no relation to gonorrhœa. In some of them, according to the history, there had been no sexual intercourse for a period of months or even years. Often there was a previous history of non-specific urethritis, and the incubation period seemed to be extremely variable. He had had patients produce a non-specific urethritis the day after risk (? activation of something latent). Others would not have been exposed to risk for weeks; the question then was whether it was related to the previous risk.

With regard to the non-infective group, calculi were sometimes a cause and a pinhole meatus might predispose to chronic urethritis. Among chemical contraceptives, quinine seemed to be a gross offender. He thought the reaction was allergic, not depending on the amount but whether it had been used at all.

Hypochondriacs seemed to be more susceptible to these discharges. He had noted urethral discharge in persons with urticaria. In some cases urethroscopy revealed "sago-grain" urethritis, and many of these cases had some chronic vesicular or prostatic infection with no evidence of gonococcal origin; in the past he had tried zinc ionisation with some success.

He had never seen a case of diabetic urethritis and asked whether it was chemical or infective (*e.g.*, yeasts).

When non-specific urethritis has followed risk a Wassermann should be carried out later to make quite sure that it was not due to syphilis. In civil practice he would take a lot of persuading to submit a person with a benign urethritis to hyperthermia.